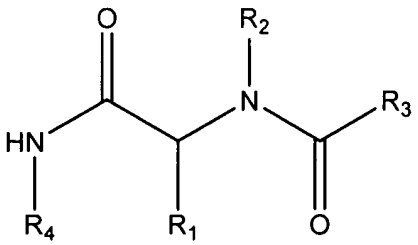
Amendments to the Claims

Please amend Claims 1, 11, 17 and 20. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

What is Claimed is:

1. (Currently amended) A method of inhibiting rejection of a transplanted organ, tissue or cell in a recipient mammal, the method comprising the step of administering to the recipient mammal an effective amount of anti-CD40L monoclonal antibody or rapamycin and an effective amount of a compound represented by the following structural formula:



or a physiological salt thereof, wherein:

R_1 is a substituted or unsubstituted aryl group, a substituted or unsubstituted aralkyl group or a substituted or unsubstituted alkyl group;

R_2 is an optionally substituted aralkyl group or an alkyl group substituted with $-NR_5R_6$;

R_3 is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;

R_4 a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group; and

R_5 and R_6 are independently selected from a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group or R_5 and R_6 taken together with the nitrogen to which they are attached are a non-aromatic heterocyclic group;

wherein each substituted aryl group, substituted alkyl group or substituted aralkyl group are independently optionally substituted at a carbon atom with-OH, -Br, -Cl, -I, -F, R, $-CH_2R$, $-OCH_2R$, $-CH_2OC(O)R$, -OR, -O-COR, -COR, -CN, $-NO_2$, -COOH, $-SO_3H$, $-NH_2$, -NHR, $-N(R)_2$, -COOR, -CHO, $-CONH_2$, -CONHR, $-CON(R)_2$, -NHCOR, -NRCOR, $-NHCONH_2$, -NHCONRH, $-NHCON(R)_2$, $-NRCONH_2$, -NRCONRH, $-NRCON(R)_2$, $-C(=NH)-NH_2$, -C(=NH)-NHR, $-C(=NH)-N(R)_2$, $-C(=NR)-NH_2$, -C(=NR)-NHR, $-C(=NR)-N(R)_2$, $-NH-C(=NH)-NH_2$, -NH-C(=NH)-NHR, $-NH-C(=NH)-N(R)_2$, $-NH-C(=NR)-NH_2$, -NH-C(=NR)-NHR, $-NH-C(=NR)-N(R)_2$, $-NRH-C(=NH)-NH_2$, -NR-C(=NH)-NHR, $-NR-C(=NH)-N(R)_2$, $-NR-C(=NR)-NH_2$, -NR-C(=NR)-NHR, -NR-C(=NR)-$N(R)_2$, $-SO_2NH_2$, $-SO_2NHR$, $-SO_2NR_2$, -SH, $-SO_kR$ [[and]] or -NH-C(=NH)-NH_2;

wherein each substituted aryl group or substituted aralkyl group are independently optionally substituted at a nitrogen atom, if present, with –R', $-N(R')_2$, -C(O)R', $-CO_2R'$, -C(O)C(O)R', $-C(O)CH_2C(O)R'$, $-SO_2R'$, $-SO_2N(R')_2$, $-C(=S)N(R')_2$, $-C(=NH)-N(R')_2$, or [[and]] $-NR'SO_2R'$;

R' is hydrogen, an alkyl group, phenyl, -O(Ph), $CH_2(Ph)$, heteroaryl or non-aromatic heterocyclic ring;

each R is independently an alkyl, benzyl, or aryl group; or $-N(R)_2$, taken together, can also form a non-aromatic heterocyclic group; and

k is 0, 1 or 2.

2. (Original) The method of Claim 1 wherein the transplanted organ, tissue or cell is a transplanted heart, kidney, lung, liver, pancreas, skin or bone marrow.

3. (Original) The method of Claim 1 wherein the mammal is the recipient of a transplanted stem cell(s).

4. (Original) The method of Claim 1 wherein the transplanted organ, tissue or cell is xenogenic or bio-engineered.

5. (Cancelled)

6. (Cancelled)

7. (Original) The method of Claim 1 wherein R_2 is an optionally substituted heteroaralkyl group or an alkyl group substituted with $-NR_5R_6$.

8. (Original) The method of Claim 7 wherein:
   a) R_1 is an optionally substituted aryl group or an optionally substituted C_1-C_4 aralkyl group;
   b) R_3 is an optionally substituted aryl group or an optionally substituted C_1-C_4 aralkyl group; and
   c) R_4 is an optionally substituted aryl group, an optionally substituted cycloalkyl group, an optionally substituted C_1-C_4 aralkyl group or an optionally substituted C_1-C_4 cycloalkylalkyl group.

9. (Original) The method of Claim 7 wherein:
   a) R_1 is an optionally substituted phenyl group or an optionally substituted phenyl-C_1-C_4 alkyl group;
   b) R_3 a substituted or unsubstituted phenyl, phenyl-C_1-C_4-alkyl, diphenyl-C_1-C_4-alkyl, pyrazolyl, pyrazolyl-C_1-C_4-alkyl, indolyl, indolyl-C_1-C_4-alkyl, thienylphenyl, thienylphenyl-C_1-C_4-alkyl, furanylphenyl, furanylphenyl-C_1-C_4-alkyl, fluorenyl, fluorenyl-C_1-C_4-alkyl, naphthyl, naphthyl-C_1-C_4-alkyl, quinoxalinyl, quinoxalinyl-C_1-C_4-alkyl, an optionally substituted quinazolinyl, an optionally substituted quinazolinyl-C_1-C_4-alkyl, pyrolyl, pyrolyl-C_1-C_4-alkyl, thienyl, thienyl-C_1-C_4-alkyl, furanyl or furanyl-C_1-C_4-alkyl; and

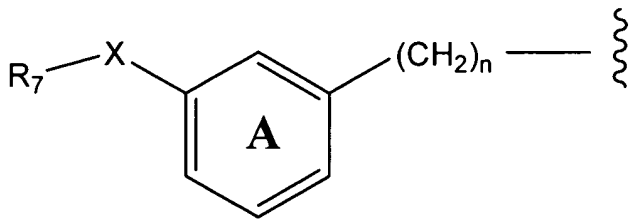
c) R_4 is an optionally substituted phenyl group, an optionally substituted phenyl-C_1-C_4-alkyl group, an optionally substituted diphenyl-C_1-C_4-alkyl group, an optionally substituted C_3-C_8-cycloalkyl-C_1-C_4-alkyl group or an optionally substituted di-(C_3-C_8-cycloalkyl)-C_1-C_4-alkyl group.

10. (Original) The method of Claim 9 wherein R_2 is an optionally substituted imadazolyl-C_1-C_4-alkyl group or a C_1-C_4 alkyl group substituted with -NR_5R_6.

11. (Currently amended) The method of Claim 10 wherein:

R_1 is a phenyl group or phenyl-C_1-C_4 alkyl group each optionally substituted with R, -CH_2R, -OCH_2R, -$CH_2OC(O)R$, -OH, halogen, -OR, -O-COR, -COR, -CN, -NO_2, -COOH, -SO_3H, -NH_2, -NHR, -$N(R)_2$, -COOR, -CHO, -$CONH_2$, -CONHR, -$CON(R)_2$, -NHCOR, -NRCOR, -$NHCONH_2$, -NHCONRH, -$NHCON(R)_2$, -$NRCONH_2$, -NRCONRH, -$NRCON(R)_2$, -C(=NH)-NH_2, -C(=NH)-NHR, -C(=NH)-$N(R)_2$, -C(=NR)-NH_2, -C(=NR)-NHR, -C(=NR)-$N(R)_2$, -NH-C(=NH)-NH_2, -NH-C(=NH)-NHR, -NH-C(=NH)-$N(R)_2$, -NH-C(=NR)-NH_2, -NH-C(=NR)-NHR, -NH-C(=NR)-$N(R)_2$, -NRH-C(=NH)-NH_2, -NR-C(=NH)-NHR, -NR-C(=NH)-$N(R)_2$, -NR-C(=NR)-NH_2, -NR-C(=NR)-NHR, -NR-C(=NR)-$N(R)_2$, -SO_2NH_2, -SO_2NHR, -$SO_2N(R)_2$, -SH or -SO_kR;

R_3 is represented by the following structural formula:



R_4 is 2,2-diphenylethyl, 2-phenylethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, benzyl, or 2-pyridylethyl, each optionally substituted with -OH, halogen, R, -CH_2R, -OCH_2R, -$CH_2OC(O)R$, -OR, -O-COR, -COR, -CN, -NO_2, -COOH, -SO_3H, -NH_2, -NHR, -$N(R)_2$, -COOR, -CHO, -$CONH_2$, -CONHR, -$CON(R)_2$,

-NHCOR, -NRCOR, -$NHCONH_2$, -NHCONRH, -$NHCON(R)_2$, -$NRCONH_2$, -NRCONRH, -$NRCON(R)_2$, -$C(=NH)-NH_2$, -C(=NH)-NHR, -$C(=NH)-N(R)_2$, -$C(=NR)-NH_2$, -C(=NR)-NHR, -$C(=NR)-N(R)_2$, -$NH-C(=NH)-NH_2$, -NH-C(=NH)-NHR, -$NH-C(=NH)-N(R)_2$, -$NH-C(=NR)-NH_2$, -NH-C(=NR)-NHR, -$NH-C(=NR)-N(R)_2$, -$NRH-C(=NH)-NH_2$, -NR-C(=NH)-NHR, -$NR-C(=NH)-N(R)_2$, -$NR-C(=NR)-NH_2$, -NR-C(=NR)-NHR, -$NR-C(=NR)-N(R)_2$, -SO_2NH_2, -SO_2NHR, -$SO_2N(R)_2$, -SH or -SO_kR;

Ring **A** is substituted or unsubstituted; R_7 is an optionally substituted phenyl, furanyl, thienyl or pyridyl group; n is an integer from 1-4; and X is a bond, CH_2, OCH_2, $CH_2OC(O)$, CO, OC(O), C(O)O, O, S, SO or SO_2;

each R is independently C_1-C_4 alkyl or phenyl optionally substituted with amino, alkylamino, dialkylamino, aminocarbonyl, halogen, alkyl, alkylaminocarbonyl, dialkylaminocarbonyloxy, alkoxy, nitro, cyano, carboxy, alkoxycarbonyl, alkylcarbonyl, hydroxy, haloalkoxy, or haloalkyl; and

k is zero, one or two.

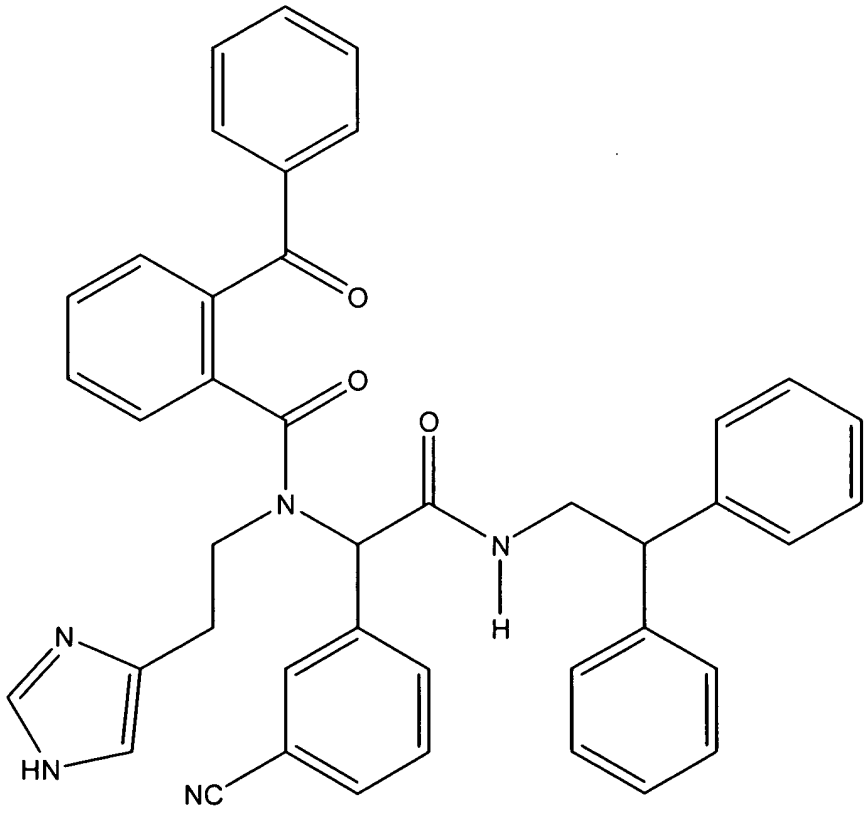
12. (Original) The method of Claim 11 wherein R_1 is a phenyl group or phenyl-C_1-C_2 alkyl group, each optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, CN, C_1-C_4-alkylthiol, C_1-C_4-haloalkyl or phenoxy; R_4 is 2,2-diphenylethyl, 2-phenylethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, benzyl, or 2-pyridylethyl, each optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, CN, C_1-C_4-alkylthiol, C_1-C_4-haloalkyl or phenoxy; R_7 is an optionally substituted phenyl group; n is 1; and X is CO.

13. (Original) The method of Claim 12 wherein Ring **A** is unsubstituted and R_7 is a phenyl group optionally substituted with R, -CH_2R, -OCH_2R, -$CH_2OC(O)R$, -OH, halogen, -OR, -O-COR, -COR, -CN, -NO_2, -COOH, -SO_3H, -NH_2, -NHR, -$N(R)_2$, -COOR, -CHO, -$CONH_2$, -CONHR, -$CON(R)_2$, -NHCOR, -NRCOR, -$NHCONH_2$, -NHCONRH, -$NHCON(R)_2$, -$NRCONH_2$, -NRCONRH, -$NRCON(R)_2$, -$C(=NH)-NH_2$, -C(=NH)-NHR, -$C(=NH)-N(R)_2$, -$C(=NR)-NH_2$, -C(=NR)-NHR, -$C(=NR)-N(R)_2$, -$NH-C(=NH)-NH_2$, -NH-C(=NH)-NHR, -$NH-C(=NH)-N(R)_2$, -$NH-C(=NR)-NH_2$, -NH-C(=NR)-NHR,

-NH-C(=NR)-N(R)$_2$, -NRH-C(=NH)-NH$_2$, -NR-C(=NH)-NHR, -NR-C(=NH)-N(R)$_2$, -NR-C(=NR)-NH$_2$, -NR-C(=NR)-NHR, -NR-C(=NR)-N(R)$_2$, -SO$_2$NH$_2$, -SO$_2$NHR, -SO$_2$N(R)$_2$, -SH or -SO$_k$R.

14. (Original) The method of Claim 13 wherein R_7 is a phenyl group; and R_2 is 2-(imidazol-4-yl)ethyl.

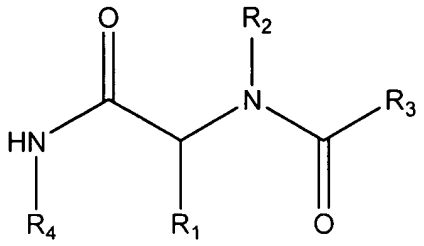
15. (Previously presented) A method of inhibiting rejection of a transplanted organ, tissue or cell in a recipient mammal, the method comprising the step of administering to the recipient mammal an effective amount of anti CD40L monoclonal antibody and an effective amount of a compound represented by the following structural formula:



or a pharmaceutically acceptable salt of the compound.

16. (Original) The method of Claim 15 wherein the transplanted organ, tissue or cell is a transplanted heart, kidney, lung, liver, pancreas, skin or bone marrow.

17. (Currently amended) A composition comprising anti-CD40L monoclonal antibody or rapamycin and a compound represented by the following structural formula:



or a physiological salt thereof, wherein:

R_1 is a substituted or unsubstituted aryl group or a substituted or unsubstituted alkyl group;

R_2 is an optionally substituted aralkyl group or an alkyl group substituted with $-NR_5R_6$;

R_3 is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;

R_4 a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group; and

R_5 and R_6 are independently selected from a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group or R_5 and R_6 taken together with the nitrogen to which they are attached are a non-aromatic heterocyclic group;

wherein each substituted aryl group or substituted alkyl group are independently optionally substituted at a carbon atom with-OH, -Br, -Cl, -I, -F, R, $-CH_2R$, $-OCH_2R$, $-CH_2OC(O)R$, -OR, -O-COR, -COR, -CN, $-NO_2$, -COOH, $-SO_3H$, $-NH_2$, -NHR, $-N(R)_2$, -COOR, -CHO, $-CONH_2$, -CONHR, $-CON(R)_2$, -NHCOR, -NRCOR, $-NHCONH_2$,

-NHCONRH, -NHCON($R)_2$, -NRCONH$_2$, -NRCONRH, -NRCON($R)_2$, -C(=NH)-NH$_2$, -C(=NH)-NHR, -C(=NH)-N($R)_2$, -C(=NR)-NH$_2$, -C(=NR)-NHR, -C(=NR)-N($R)_2$, -NH-C(=NH)-NH$_2$, -NH-C(=NH)-NHR, -NH-C(=NH)-N($R)_2$, -NH-C(=NR)-NH$_2$, -NH-C(=NR)-NHR, -NH-C(=NR)-N($R)_2$, -NRH-C(=NH)-NH$_2$, -NR-C(=NH)-NHR, -NR-C(=NH)-N($R)_2$, -NR-C(=NR)-NH$_2$, -NR-C(=NR)-NHR -NR-C(=NR)-N($R)_2$, -SO_2NH$_2$, -SO_2NHR, -SO_2NR_2, -SH, -SO_kR [[and]] or -NH-C(=NH)-NH$_2$;

wherein each substituted aryl group is optionally independently substituted at a nitrogen atom, if present, with –R', -N(R')$_2$, -C(O)R', -CO_2 R', -C(O)C(O)R', -C(O)CH_2 C(O)R', -SO_2R', -SO_2 N(R')$_2$, -C(=S)N(R')$_2$, -C(=NH)-N(R')$_2$, [[and]] or –NR' SO_2R';

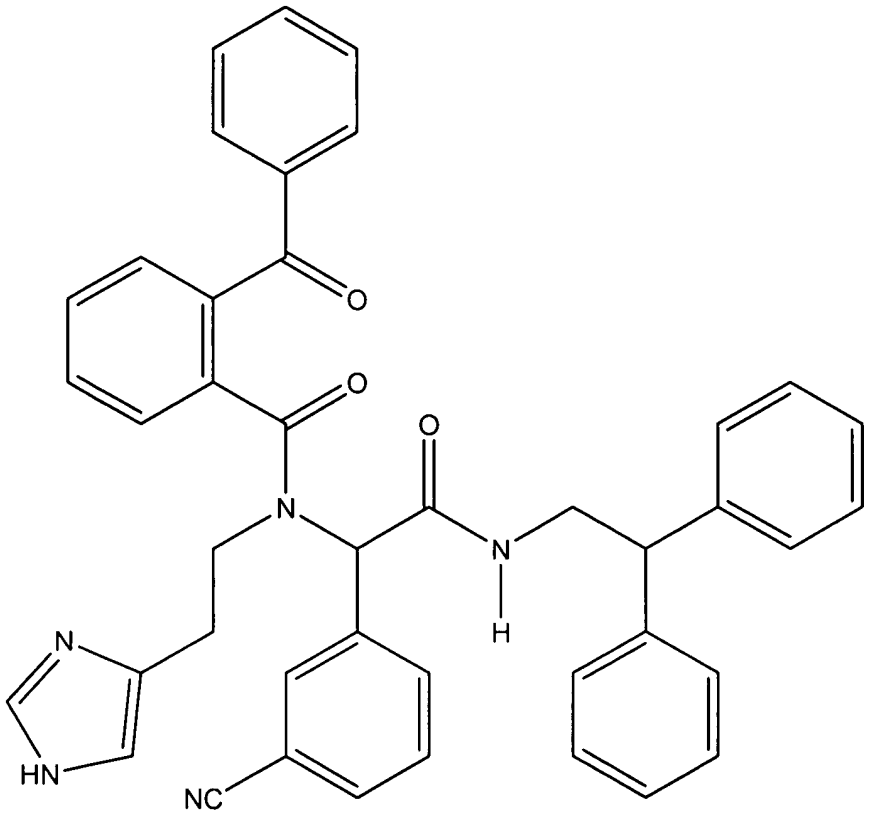
R' is hydrogen, an alkyl group, phenyl, -O(Ph), CH_2(Ph), heteroaryl or non-aromatic heterocyclic ring;

each R is independently an alkyl, benzyl, or aryl group; or -N($R)_2$, taken together, can also form a non-aromatic heterocyclic group; and

k is 0, 1 or 2.

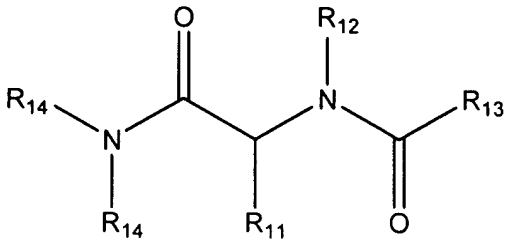
18. (Cancelled)

19. (Previously presented) A composition comprising anti CD40L monoclonal antibody and a compound represented by the following structural formula:



or a pharmaceutically acceptable salt of the compound.

20. (Currently amended) A method of inhibiting rejection of a transplanted organ, tissue or cell in a recipient mammal, the method comprising the step of administering to the recipient mammal an effective amount of anti-CD40L monoclonal antibody or rapamycin and an effective amount of a compound represented by the following structural formula:



R_{11} is -H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

R_{12} is alkyl substituted with $NR_{15}R_{16}$, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl;

R_{13} is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenonyl, or a substituted or unsubstituted cycloalkylalkyl; and

each R_{14} is independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;

R_{15} and R_{16} are independently selected from H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl or unsubstituted aralkyl or R_{15} and R_{16} together with the nitrogen to which they are attached are a heterocycloalkyl;

wherein each substituted aryl group, substituted alkyl group, substituted heteroaralkyl, substituted heterocycloalkylalkyl, substituted cycloalkylalkyl, substituted benzophenonyl, substituted cycloalkyl, heterocycloalkyl or substituted aralkyl group are independently optionally substituted at a carbon atom with-OH, -Br, -Cl, -I, -F, R, $-CH_2R$, $-OCH_2R$, $-CH_2OC(O)R$, -OR, -O-COR, -COR, -CN, $-NO_2$, -COOH, $-SO_3H$, $-NH_2$, -NHR, $-N(R)_2$, -COOR, -CHO, $-CONH_2$, -CONHR, $-CON(R)_2$, -NHCOR, -NRCOR, $-NHCONH_2$, -NHCONRH, $-NHCON(R)_2$, $-NRCONH_2$, -NRCONRH, $-NRCON(R)_2$,

$-C(=NH)-NH_2$, $-C(=NH)-NHR$, $-C(=NH)-N(R)_2$, $-C(=NR)-NH_2$, $-C(=NR)-NHR$, $-C(=NR)-N(R)_2$, $-NH-C(=NH)-NH_2$, $-NH-C(=NH)-NHR$, $-NH-C(=NH)-N(R)_2$, $-NH-C(=NR)-NH_2$, $-NH-C(=NR)-NHR$, $-NH-C(=NR)-N(R)_2$, $-NRH-C(=NH)-NH_2$, $-NR-C(=NH)-NHR$, $-NR-C(=NH)-N(R)_2$, $-NR-C(=NR)-NH_2$, $-NR-C(=NR)-NHR$, $-NR-C(=NR)-N(R)_2$, $-SO_2NH_2$, $-SO_2NHR$, $-SO_2NR_2$, -SH, $-SO_kR$ [[and]] or $-NH-C(=NH)-NH_2$;

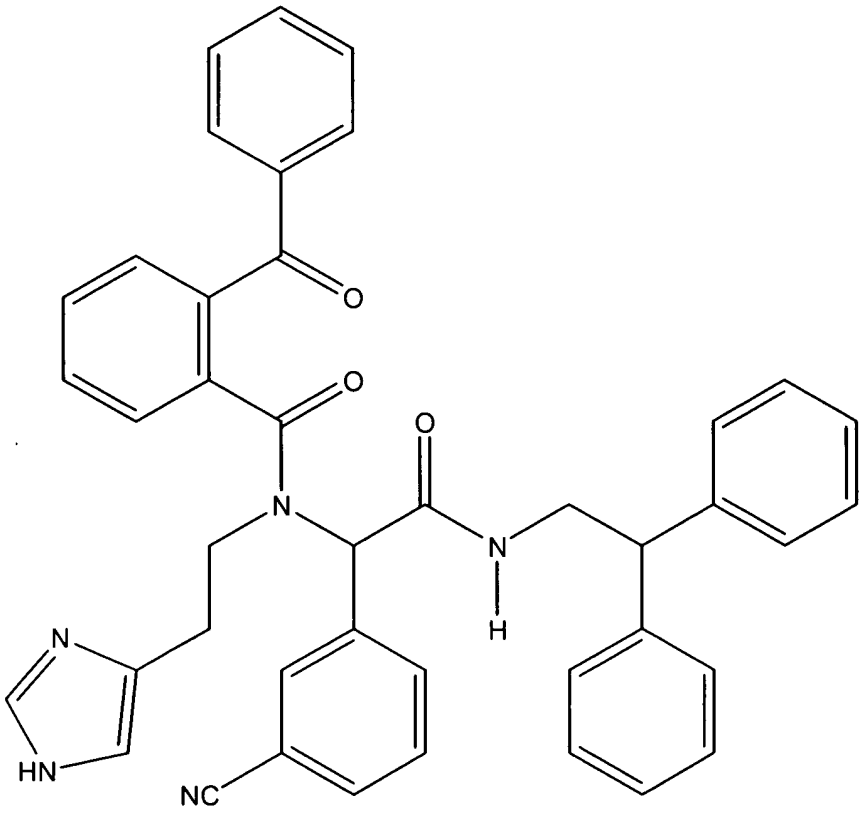
wherein each substituted aryl group, substituted heteroaralkyl, substituted heterocycloalkylalkyl, substituted cycloalkylalkyl, [[,]] heterocycloalkyl or substituted aralkyl group are independently optionally substituted at a nitrogen atom, if present, with –R', $-N(R')_2$, $-C(O)R'$, $-CO_2R'$, $-C(O)C(O)R'$, $-C(O)CH_2C(O)R'$, $-SO_2R'$, $-SO_2N(R')_2$, $-C(=S)N(R')_2$, $-C(=NH)-N(R')_2$, [[and]] or $-NR'SO_2R'$;

R' is hydrogen, an alkyl group, phenyl, -O(Ph), $CH_2(Ph)$, heteroaryl or non-aromatic heterocyclic ring;

each R is independently an alkyl, benzyl, or aryl group; or $-N(R)_2$, taken together, can also form a non-aromatic heterocyclic group; and

k is 0, 1 or 2.

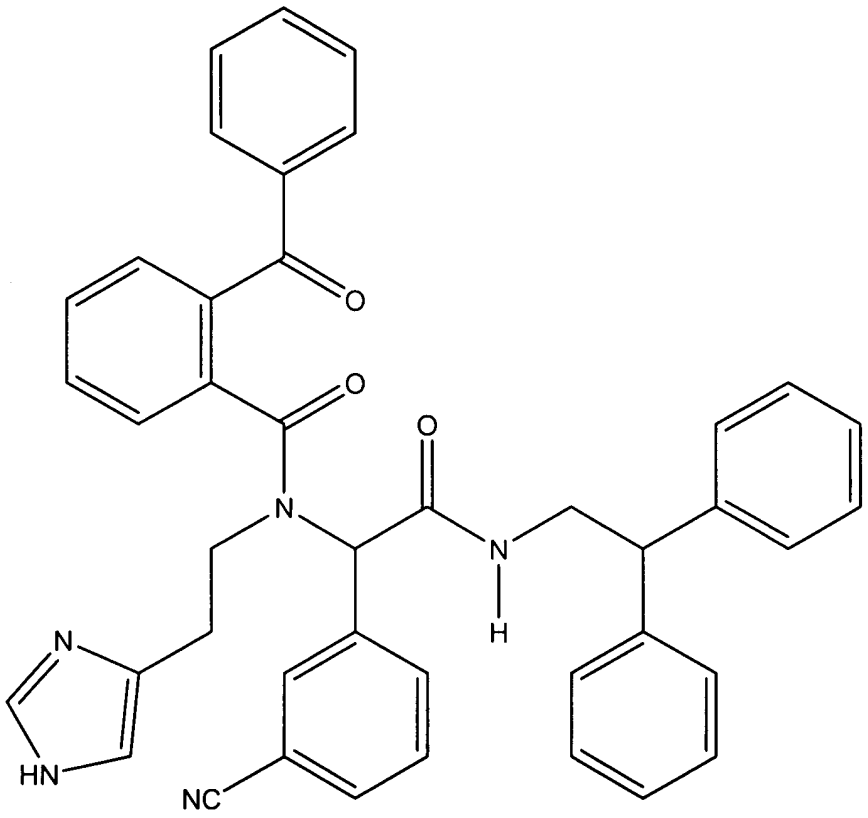
21. (Previously presented) A method of inhibiting rejection of a transplanted organ, tissue or cell in a recipient mammal, the method comprising the step of administering to the recipient mammal an effective amount of rapamycin and an effective amount of a compound represented by the following structural formula:



or a pharmaceutically acceptable salt of the compound.

22. (Previously presented) The method of Claim 21 wherein the transplanted organ, tissue or cell is a transplanted heart, kidney, lung, liver, pancreas, skin or bone marrow.

23. (Previously presented) A composition comprising rapamycin and a compound represented by the following structural formula:



or a pharmaceutically acceptable salt of the compound.